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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO. ¹
09/786,309	06/06/2001	Masayoshi Mishina	55573	8081
21874	7590	07/20/2005	EXAMINER	
EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205			BERTOGLIO, VALARIE E	
			ART UNIT	PAPER NUMBER
			1632	
DATE MAILED: 07/20/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/786,309	Applicant(s) MISHINA ET AL.	
	Examiner Valarie Bertoglio	Art. Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,10-12,18 and 20-22 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8,10-12,18 and 20-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's reply filed 05/09/2005 has been received. Claims 1-7,9 and 13-17 have been cancelled. Claims 8,12,18 and 22 have been amended. Claims 8,10-12,18 and 20-22 are pending and under consideration in the instant office action.

Claim Objections

The objections to claims 8,13, and 18 set forth in the previous office action mailed 11/01/2004 are withdrawn in light of Applicant's amendments to the claims.

Claims 8 and 18 are objected to because of the following informalities:

Claims 8 and 18 should read "plurality of base pairs" at lines 9 and 8, respectively, rather than "plurality base pairs". Appropriate correction is required.

Applicant is advised that should claim 8 be found allowable, claim 12 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 12 recites that the crosslink is introduced in to DNA region containing a pyrimidine base. This recitation is superfluous as psoralens form photoadducts at pyrimidine bases and it is, therefore, inherent, that the region of the crosslink would contain a pyrimidine base.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 8,10-12,18 and 20-22 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reason of record set forth in the office action dated 11/01/2004.

Applicant's arguments filed 03/01/05 have been fully considered and are found to be partially persuasive as set forth below.

The rejection of claims 18,20 and 22 on the grounds set forth at paragraph 3 of page 3 of the previous office action mailed 11/01/04 is withdrawn in light of Applicant's amendments to the claims.

The rejection of claim 8 (and dependent claims 10-12) for being unclear as to the metes and bounds of the phrase "around the crosslinked site" (see paragraph bridging pages 3-4 of the office action mailed 11/01/2005) is withdrawn in light of Applicant's amendments to the claim.

The rejection of claims 8,10-12,18 and 20-22 as being unclear because the metes and bounds of the term "plurality" in step (d) of claims 8 and 18 is withdrawn.

The rejection of claims 8,13 and 18 as lacking antecedent basis for the limitation "the fertilized eggs" is withdrawn in light of Applicant's amendments to the claims.

The rejection of claims 12 and 22 as being unclear because of the phrase "region containing a pyrimidine base" is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8,10-12,18 and 20-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chakrabarti (1983), Grunwald #1 (1991), Grunwald #2 (1991) taken with Thomas (1996) for reasons of record set forth on pages 4-6 of the office action mailed 11/05/2005.

Applicant's arguments have been thoroughly considered and are not persuasive.

It appears that Applicant has interpreted the rejection as being based on the grounds that one of skill in the art would be motivated to combine the use of psoralen/UV irradiation taught by Thomas with the methods of mutating sperm of Chakrabarti, Grunwald#1 and Grunwald #2 (see Applicant's remarks, page 11, paragraph 2).

In response, this is not a correct interpretation of the rejection of record. The combination of teachings does not involve the methods of mutagenizing sperm as taught by Chakrabarti, Grunwald#1 and Grunwald #2, but involves the teachings of Chakrabarti, Grunwald#1 and Grunwald #2 with respect to using mutagenized sperm to create an mutant embryo. Chakrabarti, Grunwald#1 and Grunwald #2 are not relied upon for their teachings with respect to methods of

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mutagenesis. Chakrabarti, Grunwald#1 and Grunwald #2 provide methods of making mutant animals using mutagenized sperm. They provide motivation to find alternative mutagenesis methods as gamma irradiation results in large deletions and UV alone and ENU results in point mutations, which are less desirable in terms of subsequently cloning a gene responsible for a mutant phenotype.

The argument bridging pages 10-11 of Applicant's remarks is unclear. It appears Applicant is arguing that there is no teaching that a small deletion will occur in fertilized eggs when the psoralen/UV method is used in sperm. It is unclear what relevance this has to mutagenizing sperm and using the sperm to fertilize an egg. The egg genome itself does not need to be mutagenized. It, the sperm, or the egg it fertilizes, must merely comprise the recombination repair mechanism essential to biological organisms (see specification at page 7, lines 1-3) that removes the psoralen-crosslinked DNA. There is no evidence of record that a fertilized vertebrate egg would not have this recombinational repair mechanism that results in excision of the psoralen crosslink in the sperm DNA. Furthermore, gamma irradiation, like psoralen, results in double stranded breaks and uses the same double stranded break repair mechanism as psoralen. This mechanism was shown by Chakrabarti to be effective in gamma-irradiated sperm used to fertilize eggs and resulted in transfer of a deletion mutation into the offspring. Therefore, the rejection is maintained for reasons of record.

Claims 8,10-12,18 and 20-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chakrabarti (1983), Grunwald #1 (1991), Grunwald #2 (1991) taken with Yandell for reasons of record set forth on pages 6-8 of the office action mailed 11/05/2005.

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Applicant's arguments have been thoroughly considered and are not persuasive.

Applicant has argued that *C. elegans*, taught by Yandell, is not a vertebrate, as required by the claims. In response, the Yandell reference is not used for its teachings with respect to *C. elegans*, per se, but for the use of psoralen as a mutagen.

The DNA of *C. elegans*, whether in an intact organism, in a cell, or in vitro, is structurally the same as that of a vertebrate animal and its sperm. UV-irradiated, psoralen-treated sperm would be expected to have the same types of mutations as similarly treated DNA of another organism or cell or cell extract. According to Applicant's own specification, DNA recombinational repair that is essential to biological organisms (zebrafish and *C. elegans* are biological organisms), is responsible for the resulting mutation by excising the psoralen crosslinked DNA. There is no evidence of record that a fertilized vertebrate egg and the descendent cells would not have this recombinational repair mechanism that results in excision of the psoralen crosslink in the sperm DNA.

The rejection is maintained for reasons of record.

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Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

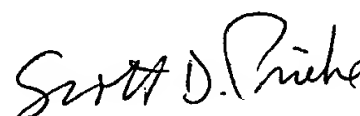
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER